PB83-250472

Event-Related Slow Brain Potential Changes in Asymptomatic Children with Secondary Exposure to Lead

(U.S.) Health Effects Research Lab.
Research Triangle Park, NC

1983

U.S. Department of Commerce
National Technical Information Service
NTIS

PB83-250472

EPA-600/D-83-104
August 1983

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NATIONAL TECHNICAL
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TECHNICAL REPORT DATA

(Please read Instructions on the reverse before completing)

1. REPORT NO.	2.	3. RECIPIENT'S ACCESSION NO.
EPA-600/D-83-104		PB83 250472

4. TITLE AND SUBTITLE	5. REPORT DATE
Event-related slow brain potential changes in asymptomatic children with secondary exposure to lead	1983
	6. PERFORMING ORGANIZATION CODE

7. AUTHOR(S)	8. PERFORMING ORGANIZATION REPORT NO.
David Otto, Vernong Benignus, K. Muller, C. Barton and P. Mushak	

9. PERFORMING ORGANIZATION NAME AND ADDRESS	10. PROGRAM ELEMENT NO.
United States Environmental Protection Agency MD-58, HERL/NTD/NPB RTP, NC 27711	11. CONTRACT/GRANT NO.

12. SPONSORING AGENCY NAME AND ADDRESS	13. TYPE OF REPORT AND PERIOD COVERED
Health Effects Research Laboratory Office of Research and Development U.S. Environmental Protection Agency Research Triangle Park, NC 27711	14. SPONSORING AGENCY CODE EPA/600/11

15. SUPPLEMENTARY NOTES

16. ABSTRACT

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17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group

18. DISTRIBUTION STATEMENT	19. SECURITY CLASS (This Report)	21. NO. OF PAGES
Release to Public	Unclassified	10
	20. SECURITY CLASS (This Page) Unclassified	22. PRICE

EPA Form 2220-1 (Rev. 4-77) PREVIOUS EDITION IS OBSOLETE

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EVENT-RELATED SLOW BRAIN POTENTIAL CHANGES IN ASYMPTOMATIC CHILDREN WITH SECONDARY EXPOSURE TO LEAD

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ABSTRACT

Slow cortical potentials were studied in young children with blood lead (PbB) levels ranging from 6 to 52 µg/dl. Slow wave (SW) voltage recorded from the scalp during sensory conditioning varied as a linear function of PbB level and age. Evidence of a persistent alteration of brain function was also found in a two-year follow-up assessment of the children.

KEYWORDS

Developmental neurotoxicology, body lead burden, slow brain potentials, sensory conditioning, CNS function.

INTRODUCTION

Children are at greater risk than adults for brain damage from lead (Pb) exposure due to increased vulnerability of the immature brain, greater absorption rate of ingested Pb, and pica behavior -- the tendency of young children to eat nonfood substances (e.g., dirt or paint chips) that contain Pb (USEPA, 1977). Although the prevalence of childhood lead poisoning has been steadily decreasing in the United States since the use of Pb in household paint was banned, inadvertent contamination of homes by workers in lead industries still poses a significant threat to young children (Dolcourt et al, 1978). Increasing evidence suggests that asymptomatic Pb exposures (i.e., blood Pb levels below 60 µg/dl) in young children are associated with subtle learning and developmental disorders (Needleman, 1980). This evidence clearly emphasizes the need for rigorous enforcement of appropriate hygienic procedures where workers handle or are exposed to Pb compounds.

Results of a preliminary study of the effects of asymptomatic Pb exposure on central nervous system function in young children will be reviewed here. These findings have been reported in more detail elsewhere (Otto, et al., 1981, and Benignus et al, 1981). Results of a two-year

year follow-up study of a subgroup of these children will also be reviewed. About half of the children in this study came from homes in which the parent(s) worked in a lead battery factory. Pb exposure in other children resulted from the ingestion of paint chips. Results indicated that slow wave (SW) voltage during sensory conditioning varied as a linear function of PbB level and age. Evidence of persistent changes in brain function was found in a subset of the children studied two years later.

METHODS

One hundred children (53 boys) aged 13 - 75 months participated in this study. Most children were from low-income Black families. All children were asymptomatic at the time of study. This study was part of a comprehensive neurobehavioral evaluation carried out at North Carolina Memorial Hospital. Pediatric and neurological examinations were administered and extensive demographic data were obtained from parent interviews.

Body Pb burden was determined from blood samples obtained from children on the day of evaluation. PbB levels were analyzed by flame atomic absorption spectrometry using the Delves-cup method (Delves 1970).

Silver-silver chloride electrodes were used to record EEG from Fpz, Cz, P3 and P4 referred to linked mastoids. The frontal electrode was used to monitor vertical eye movements. EEG was low-pass filtered at 30 Hz (3 dB down). Amplifiers were modified to yield an 8 sec time-constant. Trials with eye movements, blink, blocking, muscle or other artifacts were eliminated from averages computed off-line.

Testing was done in a small acoustic chamber. Children under 48 months usually sat in the lap of an adult. Cartoons were used to engage the attention and minimize eye/body movement artifact. In order to test very young children, a classical conditioning paradigm that required no verbal instruction or motor response was employed. A 30 msec 2 KHz tone (conditional stimulus) was paired with a 1.5 sec blackout (unconditional stimulus) of the cartoon. An electromechanical shutter attached to the movie projector was used to produce the blackout period which commenced 1.5 sec after tone onset. The tone occurred pseudorandomly every 12 - 22.5 sec.

Data from 41 children were used in the analysis. Subjects were rejected for a variety of reasons including medical, technical, or behavioral problems. At least 10 artifact-free trials were required for individual subject data to be included in the analysis. Only 13 children under 36 months of age satisfied criteria for inclusion. Slow wave (SW) amplitude was computed as the mean voltage of a 1 sec interval preceding the blackout period relative to a 350 msec pre-tone baseline. Statistical analysis was limited to the vertex in order to maximize the power of tests given a fixed α level. A stepwise multivariate procedure was used to evaluate results (see Otto et al., 1981).

RESULTS

Table I summarizes the results of the regression analysis. SW voltage varied as a linear function of PbB, but the slope of this function changed systematically with age. For children under 5 years of age, SW voltage

tended to be positive at low PbB levels, but to be increasingly negative above 30 µg/dl. For children over 5 years of age, SW voltage tended to be negative at low PbB levels and less negative or even positive above 30 µg/dl. The interactive effects of age and PbB on SW voltage are illustrated in Fig. 1.

Table I. Results of Multivariate Regression Analysis

SOURCE	DF(num)	DF(den)	F	p <
Demographics	3	37	1.66	.20
Age Main Effect	3	37	.27	.85
PbB Main Effect	3	37	2.49	.08
Age x PbB Interaction	4	36	3.08	.028

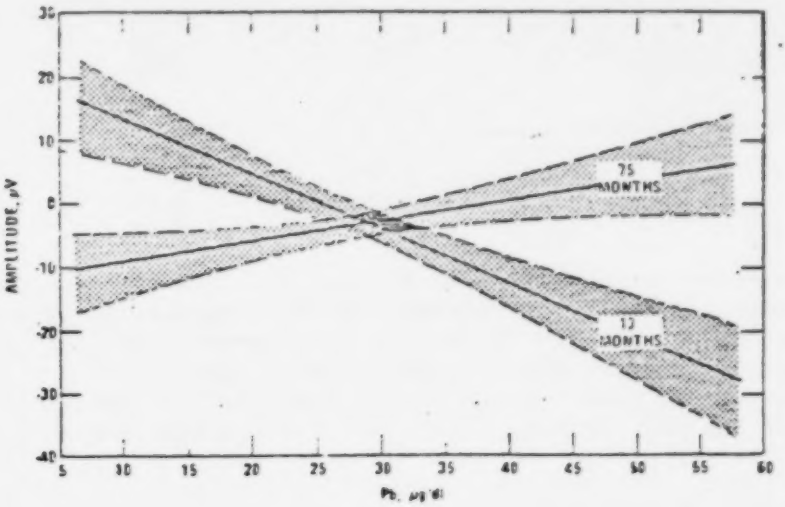

Fig. 1. Interactive effects of age and PbB levels on slow wave voltage during tone-shutter conditioning. Predicted SW amplitude and 95% confidence bounds are depicted in 13 and 75 month old children as a function of PbB. (Redrawn from Electroenceph. Clin. Neurophysiol., 1981, 52:235.)

TWO-YEAR FOLLOW-UP ASSESSMENT

Do the effects of early lead exposure in children persist over time? To answer this question with respect to slow wave voltage, a subset of the children was brought back for a two-year follow-up assessment. Several minor changes in procedures were made: more trials were recorded in the sensory conditioning paradigm to improve the signal-to-noise ratio of slow potential averages and a video cassette system was used in lieu of a movie projector to present cartoons.

Twenty-eight children (19 boys) aged 35 to 95 months participated in the follow-up study. The ranges of PbB levels were 6-55 µg/dl in the original study and 14-39 µg/dl in the follow-up study. Only three children were found to have PbBs > 30 µg/dl at follow-up. Other procedures were as described above.

TABLE II. MULTIVARIATE REGRESSION ANALYSIS OF AGE, BLOOD LEAD LEVEL (PbB1), AND SLOW WAVE VOLTAGE DURING SENSORY CONDITIONING

Source	df(num,den)	F	p<
Overall Multivariate test	6,46	3.05	0.014
All trials (1-100)			
Age	1,24	0.56	0.47
PbB1	1,24	6.97	0.015
Age X PbB1 Interaction	1,24	4.60	0.05
Early trials (1-40)			
Age	1,24	0.38	0.55
PbB1	1,24	0.09	0.76
Age X PbB1 Interaction	1,24	0.02	0.90
Late trials (41-100)			
Age	1,24	2.64	0.12
PbB1	1,24	6.23	0.02
Age X PbB1 Interaction	1,24	6.39	0.02

Table II shows the results of the multivariate analysis of slow wave voltage recorded at the vertex. SW voltage was regressed on PbB1 values obtained in the original study in order to determine if there was any residual effect of early exposure. A significant age x PbB1 interaction was observed in SW measures derived from individual averages across all artifact-free trials (1-100). The main effect of PbB1, but not of age, was also significant. The data were broken down into early (1-40) and late (41-100) trials to assess the time course of the overall effect. This breakdown revealed that the effects were present in the late trials only. Fig. 2 shows predicted SW voltage and 95% confidence bands plotted as a function of original PbB levels for the extreme ages represented in the follow-up sample.

DISCUSSION

SW voltage varied as a linear function of PbB level within an observed range of 7-52 µg/dl. The relationship of PbB and SW voltage is of particular interest since the data suggest that even very low levels of body Pb burden affect this parameter of brain function, i.e., a 'no effect' threshold does not appear to exist. These data represent the lowest PbB

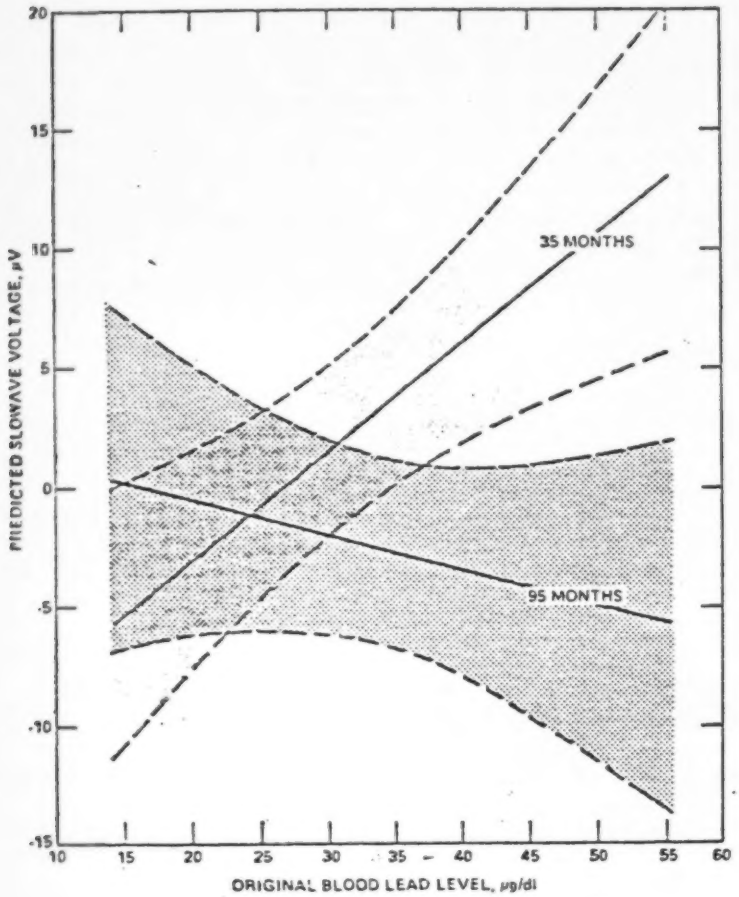

Fig. 2. Predicted SW voltage and 95% confidence bounds in 35- and 95 month old children in two-year follow-up group plotted as a function of original blood Pb level.

effect level ever observed in relation to CNS function. The only other biological function known to be affected at such low PbB levels is heme synthesis. Delta-aminolevulinic acid dehydratase activity is inhibited in children and adults at 10 μg/dl (Hernberg et al. 1970).

The slow wave observed in this study is presumed to be an index of sensory conditioning. The results, therefore, imply that Pb exposure may alter conditioning or learning in children. The effect of Pb on this electrophysiological parameter has not been studied in animal models, although impairments in operant conditioning or maze learning have been reported in several species exposed to Pb (USEPA 1977). Whether the effects are due to a general learning or specific sensory deficit has not been resolved. Fox et al. (1977) observed increased latencies in both primary and secondary components of visual evoked potentials (VEPs) of rats exposed neonatally to Pb. Results of Fox et al. suggest that both sensory and associative levels of CNS function are affected by Pb exposure since primary visual components are considered to reflect activity in specific sensory pathways, while sec-ondary visual components are considered to reflect activity in nonspecific pathways associated with attention, perception and learning.

Results of the two-year follow-up assessment suggest that the linear relationship of SW voltage and body Pb burden persists over time, despite a considerable drop in the mean PbB level of the children. These findings coupled with our original observations provide compelling support for the continuum view of Pb effects on central nervous system function. The current conception of a "safe threshold" for body Pb burden in children clearly requires a careful reappraisal. These results also reinforce the need for rigorous monitoring of worker hygiene habits to prevent the inadvertent transmission of Pb dust into the home with the consequent risk of central nervous damage to young children.

ACKNOWLEDGEMENT

Supported by NIEHS Grant #ES-01104, EPA Contract #68-02-1702, USPHS Grant #HD-03110 to the Child Development Research Institute; MCH Project 916 to the Division for Disorders of Development and Learning, and the Wake County Public Health Department. The cooperation of S. Schroeder, C. Milar, J. Dolcourt and the technical assistance of J. Nichols, J. Prah, and k. Seiple are gratefully acknowledged.

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